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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,235	BLONDER ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7,9-37,39-44,148 and 149* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-7,9-37,39-44,148 and 149* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Reopen

Upon reconsidering the pending claims and in view of applicants' argument file on April 21, 2005, the finality of the previous office action removed, and a new ground rejection is made on the record. This is reopen prosecution because after reconsidering the claimed invention. Office apologize any inconveniency that brought by this reopen practice.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1, 4-7, 9-37, 39-44 and 148-149 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Alonso et al. (EP 0860 166A1) in view of Hale et al. (US patent No. 5, 607,691A) and Viegas et al. (a: US Patent No. 5,300,295A).

3. Claimed invention is drawn to a composition comprising an antigen, preferably a tetanus toxoid antigen (0.0001-5% w/w), a polyoxyalkylene block copolymer (5 to 33% w/w), a non-alum adjuvant (0.01-10.0% w/w) and an aqueous liquid (60-65%w/w), wherein the viscosity of the composition increase as the temperature increase within the range of 1°C to 37 °C. At the lower temperature, the composition is in the liquid form. Moreover, the composition is by the form of disperse droplet in a mist produced by a nedulizer.

4. Alonso et al. teach a method for formulating an immunogenic composition comprising an antigen with an adjuvant chitosan and a polyoxyalkylene block copolymer in a liquid form, wherein the polyoxyalkylene block copolymer is PEO-POP, which is the same copolymer as it is taught in the current specification (The claimed reverse-thermal gelation polymers includes certain polyethers, preferably polyxyakylen block copolymers with more preferred polyxyalene

block copolymer including polyoxyethylene-polyoxypropylene block copolymers referred to herein as POE-POP block polymers, such as Pluronic TM F68, PluronicTMF127, PluronicTML121. Please see line 13 on page 17 through line 9 on page 18). Alonso et al. also disclose that the proportions of each active ingredient varied according to the size of the nanoparticle, some of the changes are within the claimed range. For example, the composition having the nanoparticle with the size of 685±27 comprising about 0.14% (w/w) of chitosan, 0.014% (w/w) of tetanus toxoind, 0.02% (w/w) sodium triphosphate, 7% (w/w) of PEO-PPO and 93% (w/w) water (See Table 1 on page 6 and Example 4 on page 5). Moreover, Alonso et al. teach that the active ingredient can be selected from any peptide, protein, polysaccharides or polynucleotide that exhibits an antigenic activity and the total weight of the copolymer may vary from 0% to 60%. (Claims 6-13). Alonso et al. do not teach to delivery the composition with a disperse droplet in a mist produced by a nedulizer.

5. Viegas et al. teach that the polypropylene/polyxyethylen block polymer formulated either as $HO(C_2H_4O)_b(C_3H_6O)_a(C_2H_4O)_bH$ or $H(OC_2H_2CH_2)_b(OCHCH_2)CH_{3a}(OC_2H_2CH_2)_bOH$ is characterized as a heat sensitive polymer, in which the copolymer is in liquid form at room temperature or below and in gel form with a desired osmolality at mammalian body temperature (Claims 1-23). It is well known in the art that mammalian body temperature is 37 °C.

6. Hale et al. explicitly teach that method for preparing and delivering a pharmaceutical composition comprising a therapeutic agent imbedded with copolymers of polyethylenes (see lines 45-55 on col. 47) that is produced as an inhaler or nebulizer or in a mist of spryer suitable for the transmucosal delivery (See lines 11-25 on col. 53), wherein the composition may be produced as a dry powder or an inhaler or a nebulizer or in a mist sprayer (See entire document, especially Table 2 on col. 15-16).

7. Regarding to the different proportion of the ingredient, MPEM cites: ***Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."*** *In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) and see*

*also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("**The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.**"); and In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes, which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar* proportions.). The modification of a working condition is generally recognized as being within the level of the ordinary skill in the art, because it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the workable ranges involves only routine skill in the art, In re Rose, 105 USPQ 237 (CCPA 1995) and In re Aller, 105, USPQ 233.

8. Therefore, it would have been obvious for a person with an ordinary skill in the art to be motivated in order to make an immunogenic composition by their need by modifying the concentrations of each ingredient to produce a desired an immune response as it is need absence unexpected result. Because once it is approve that temperature reverse copolymer can be used for delivering an antigen as an immunogenic composition.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 31, 33-44 and 148-149 are rejected under 35 U.S.C. 112; first paragraph, because the specification, while being enabling for making an immunogenic composition as an aqueous liquid, which comprises 200Lf/ml tetanus toxoid, copolymer Fluronic F127 in 16.25% (w/w), 05% 9w/w) adjuvant chitosan, does not reasonably provide enablement for making any or all immunogenic composition as an aqueous liquid with any or all kind of polyoxyalklen block copolymer in any percent, any active adjuvant in any concentration. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

11. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

12. Nature of the invention is directed to an aqueous solution of an immunogenic composition, wherein the composition is made by 200Lf/ml tetanus toxoid, copolymer Fluronic F127 in 16.25% (w/w), 05% 9w/w) adjuvant chitosan.

13. Scope of claims: The scope of claims read on an immunogenic composition made by an antigen with any or all kinds of polyoxyakylene block copolymer, any non-alum adjuvant, and an aqueous liquid, that the copolymer is substantially dissolved in the aqueous phase.

14. State of art and unpredictability: The state of art teaches that an immunogenic composition can be made with an polyoxyakylene block copolymer and an adjuvant. However, lot of such copolymer is water insoluble as evidenced by Hunter et al. (J. Immunol. 1984, Vol. 133, No. 6, pp. 3167-3173, see table 1 on page 3168). Moreover, the experts, like Allison A. (METHODS 1999, Vol. 19, pp. 87-93) teaches that the copolymer L121 prepared in an adjuvant squalane emulsion adheres to the oil phase and does not dissolve in the aqueous phase. Therefore, it is unpredictable that claimed any or al copolymer can be used for preparing an aqueous immunogenic composition with any or all active adjuvant.

15. Amount of working example and guidance presented in the specification. Applicants only teach that an immunogenic composition with thermal reverse and substantial water soluble characteristics can be made by 200Lf/ml tetanus toxoid, copolymer Fluronic F127 in 16.25% (w/w), 05% 9w/w) adjuvant chitosan. The specification does not provide an adequate teaching and guidance to support the broadly claimed invention.

16. There are thousands molecule that belong to the polyoxyalene block copolymer and its derivative. However, most of them are not water-soluble. it must be considered in order to be

able the full scope of claimed invention, whether a skilled artisan would have to conducted undue and excessive experimentation.

17. After the analysis as described above, it is concluded that in order to practice the full scope of the claimed invention, an undue experimentation would have to be required.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao Qun Li
06/15/2005

James C. Housel
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